SYNTHESIS OF 4-STYRYL-2,3-DIHYDRO-1H-1,5-BENZODIAZEPIN-2-ONES

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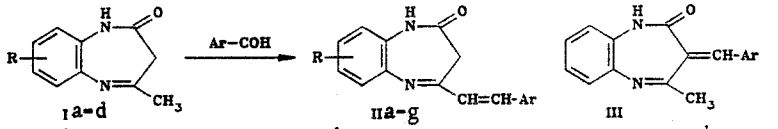
4-Styryl-2,3-dihydro-1H-1,5-benzodiazepin-2-ones were synthesized and their structure was established by means of PMR spectra and mass spectroscopy.

There is no unequivocal information on the structure of the reaction products of 4-methyl-2,3-dihydro-1H-1,5-benzodiazepin-2-ones (Ia-d) with aromatic aldehydes. It was shown in [1-3] that it is not the methylene group but the methyl group that enters the reaction to form 4-styryl-2,3-dihydro-1H-1,5-benzodiazepin-2-one (IIa). Recently [4], it was reported that, according to certain chemical transformations, compounds IIe, g are 3-arylidene derivatives III. However, the authors did not prove the structure of the compounds obtained.



I a R=H, b R=8-Cl, c R=8-CH_3O, d R=7-NO_2; II a. R=H, Ar=C_6H_5, b R=8-Cl, Ar=C_6H_5, c R=8-CH_3O, Ar=C_6H_5, d R=7-NO_2, Ar=C_6H_5, e R=H, Ar=4-NO_2—C_6H_4, f R=H, Ar=3-NO_2—C_6H_4, g R=H, Ar=4-$(CH_3)_2N$—C_6H_4

Since compounds of type II, recommended as durable dyes for nitrone [5], have a tranquilizing effect [2], and are also complexing agents [6], we decided to investigate these contradictions.

The condensation of diazepinones I with aromatic aldehydes proceeds in absolute benzene or alcohol in the presence of piperidine. It is a methyl group that enters into the reaction and not the methylene groups of diazepinone, while under these conditions 4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-2-one does not react with aldehydes. The higher reactivity of the methyl group can possibly be explained by the fact that under the influence of the nitrogen of a pyridine type heterocycle, its CH-acidity increases and in a basic medium it can form an anhydrobase [7].

There are three absorption maxima in the UV spectra of the compounds synthesized. The long-wave maximum is much more intense than that in the initial diazepinone [8] and undergoes an appreciable bathochromic shift, which indicates increase in the conjugation chain.

In the PMR spectra of compounds IIa-g, singlets of methylene protons are observed in the 3.7-4.2 ppm region, and proton signals of the methyl group are absent, which confirms their participation in the condensation reaction. The signals of the methine protons resonate in the region of the aromatic ring protons (6.8-8.5 ppm), as indicated by the ratio of the integral intensities of the signals.

The mass spectral fragmentation of compounds IIa-g also confirms the presence of a styryl group at the 4-position. It is known that for these systems, one of the most specific trends of fragmentation is the rupture of the lactam bond, followed by splitting of a ketene molecule and formation of a benzimidazolium cation [M − 42] [9].

In the mass spectrum* of compound IIa, intense peaks of M^+ 262 (55) and $[M-1]^+$ 261 (100) are observed. The main path of the fragmentation is splitting of a ketene molecule — the $[M-43]^+$ ion 220 (61). In the mass spectrum of diazepinone IIb, there are peaks of M^+,

*Here and below, m/z values are given for the peaks of ions, while the intensity in relation to the maximal peak is given in brackets.

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TABLE 1. Characteristics of Compounds Synthesized

Compound	T_{mp}, °C* (from ethanol)	R_f	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIb	209—210	0,64	68,4	4,7	9,6	$C_{17}H_{13}ClN_2O$	68,8	4,5	9,4	39
IIc	177—179	0,33	73,4	5,3	9,8	$C_{18}H_{16}N_2O_2$	74,0	5,5	9,6	41
IId	205—206	0,30	66,0	4,2	13,4	$C_{17}H_{13}N_3O_3$	66,4	4,2	13,7	28
IIf	245—246	0,31	66,7	4,3	13,5	$C_{17}H_{13}N_3O_3$	66,4	4,2	13,7	49

*Melting points: of compound IIa) 218-219°C, according to the data in [1], 218-219°C, IIe) 250-251, according to the data in [4], 250°C, IIg) 317-319°C, according to the data in [4], 320°C.

$[M - 1]^+$, $[M^+ - Cl]$, $[M^+ - HCl]$, and $[M^+ - 42]$. In the mass spectrum of the nitro derivative IIe, in contrast to the case of the mass spectrum of compounds IIa, b, the peak of the molecular ion, and not that of the $[M^+ - 1]$ ion is the basic peak. Its characteristic feature is splitting of the nitro and nitroso groups. If the arylidene substituent were present in these compounds at the 3-position, there would be no splitting of ketene, and the [M − CO–CH=CH–Ar] ion would be fairly intense in the spectrum. The intensity of this ion with m/z 131 in the mass spectra of compounds IIa, b, e does not exceed 1-2%.

EXPERIMENTAL

The UV spectra were measured on a Specord UV-vis spectrophotometer at a concentration of the materials of 10^{-4}-10^{-5} M in ethanol. The PMR spectra were recorded on a Tesla BS-567A spectrometer (100 MHz) in trifluoroacetic acid using HMDS as internal standard. The mass spectra were recorded on a MX-1303 mass spectrometer with direct introduction of the sample into the ionic source, at an input temperature 20-30°C lower than the melting points of the compounds studied. The course of the reaction and the purity of the initial and synthesized compounds were controlled on Silufol UV-254 plates in a 7:3 benzene–ethyl acetate system.

General Method for Preparation of 4-Styryl-2,3-dihydro-1H-1,5-benzodiazepin-2-ones (IIa-g). A. A 0.024 mole portion of an aromatic aldehyde and three drops of piperidine are added to a solution of 0.02 mole of diazepinone Ia-d in 15 ml of absolute benzene. The mixture is boiled for 12 h, and then cooled. The precipitate is washed with ethanol, dried and recrystallized from ethanol.

B. Two drops of piperidine are added to a solution of 0.01 mole of diazepinone Ia-d and 0.012 mole of aromatic aldehyde in 20 ml of absolute ethanol and the mixture is boiled for 3 h. The solvent is distilled, the residue is washed with ethanol and compounds IIa-g are isolated.

The physical constants and yields of the compounds obtained are listed in Table 1.

4-Styryl-2,3-dihydro-1H-1,5-benzodiazepin-2-one (IIa). UV spectrum, λ_{max} (log ε): 225 (4.34), 301 (4.33), 336 nm (4.26). PMR spectrum: 3.90 (2H, s, CH_2); 7.27-8.32 (11H, m, aromatic and methine protons); 9.82 ppm (1H, s, NH). Mass spectrum*: 262 (55; M^+), 261 (100), 221 (12), 220 (61), 219 (17), 149 (16), 129 (13), 122 (21), 119 (26), 105 (41), 97 (20), 91 (23), 83 (22), 81 (20), 77 (40).

8-Chloro-4-styryl-2,3-dihydro-1H-1,5-benzodiazepin-2-one (IIb). UV spectrum, λ_{max} (log ε): 212 (4.42), 304 (4.29), 340 nm (4.26). PMR spectrum: 4.05 (2H, s, CH_2); 7.34-8.50 (10H, m, aromatic and methine protons); 9.86 ppm (1H, s, NH). Mass spectrum: $296^\dagger$ (63; M^+), $295^\dagger$ (100), $254^\dagger$ (59), 218 (26), 188 (27), 173 (20), 149 (19), 128 (19), 127 (11), 115 (12), 109 (11), 102 (12), 91 (28), 77 (43).

4-(p-Nitrostyryl)-2,3-dihydro-1H-1,5-benzodiazepin-2-one (IIe). UV spectrum, λ_{max} (log ε): 227 (4.43), 321 (4.28), 355 nm (4.27). PMR spectrum: 4.04 (2H, s, CH_2); 7.32-8.40 (10H, m, aromatic and methine protons); 9.85 ppm (1H, s, NH). Mass spectrum: 307 (100; M^+), 306 (60), 278 (13), 277 (50), 276 (71), 266 (24), 265 (88), 262 (20), 261 (48), 235

*Peaks of M^+ and ions with an intensity > 10% are given.
†Ions containing the ^{35}Cl isotope.

(30), 234 (16), 233 (14), 220 (29), 219 (80), 218 (39), 205 (16), 204 (13), 188 (88), 173 (61), 151 (20), 150 (20) 149 (66), 132 (27), 128 (22), 127 (20), 117 (38), 116 (25), 115 (35), 105 (32), 91 (31), 77 (46).

LITERATURE CITED

1. S. Motoki, C. Urakawa, A. Kano, V. Fushimi, T. Hirano, and K. Murato, Bull. Chem. Soc. Jpn., 43, 809 (1970).
2. A. A. Stolyarchuk, Yu. N. Furman, V. L. Pikalov, Z. F. Solomko, and V. S. Tkachenko, Khim.-Farm. Zh., 9, 19 (1975).
3. L. K. Mushkalo, I. B. Dzvinchuk, and N. N. Mushkalo, Ukr. Khim. Zh., 45, 231 (1979).
4. A. K. El-Shafei, H. S. El-Kashef, and A. M. El-Khawage, Indian J. Chem., Vol. No. 21B, 655 (1982).
5. R. C. Harris and J. M. Straley, French Pat. No. 4537757; Chem. Abstr., 73, 100054 (1970).
6. N. N. Mushkalo, N. O. Markova, and L. K. Mushkalo, Vestn. Kazan. State Univ., No. 21, 31 (1980).
7. T. V. Stupnikova, B. M. Zemskii, R. S. Sagitullin, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 3, 291 (1982).
8. T. G. Chmilenko, Z. F. Solomko, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 4, 525 (1977).
9. A. N. Kost, P. A. Sharbatyan, P. B. Terent'ev, Z. F. Solomko, V. S. Tkachenko, and L. G. Gergel', Zh. Org. Khim., 8, 2113 (1972).

REACTIONS OF 4,5-DIAMINO-3-METHYL-1-PHENYLPYRAZOLE WITH DIARYLIDENEACETONES

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The reaction of 4,5-diamino-3-methyl-1-phenylpyrazole with dibenzylideneacetone and its 4,4'-derivatives has been studied; the reactions lead to aromatic 1H-2,3-dihydropyrazolo[5,4-b]1,5-diazepine derivatives. The reaction pathway has also been identified.

The reactions of aromatic and heterocyclic 1,2-diamines with α,β-unsaturated ketones constitute a direct method for the synthesis of annelated 2,3-dihydro-1,5-diazepines [1-3]. In a preceding communication [4], it was shown that 4,5-diamino-3-methyl-1-phenylpyrazole also reacts with chalcones in acidic media to give 1H-2,3-dihydropyrazolo[5,4-b]-1,5-diazepine derivatives.

Continuing these investigations, we have examined the reaction of 4,5-diamino-3-methyl-1-phenylpyrazole (I) with diarylideneacetones. In the case of the reaction of diamine I with symmetrically substituted diarylideneacetone derivatives (R = R^1), pure dihydropyrazolodiazepine derivatives (II-VII, XVIII) are obtained in excellent yield; non-symmetrical ketones (R ≠ R^1), on the other hand, give mixtures of two isomeric dihydropyrazolodiazepines, which are difficult to separate (the formation of mixtures was suggested, first of all, by the relatively low melting points of the products which were obtained, and, secondly, by analysis of their PMR spectra).

The structures of the newly synthesized compounds II-XX were confirmed on the basis of their elemental analyses and spectral characteristics (Tables 1-3). For example, the IR

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